STIC-ILL

From: Helms, Larry
Sent: Monday, December 06, 1999 2:20 PM
T : STIC-ILL
Subject: 08/940544

please send a copy of the following to Larry Helms at CM-1, 8d08, AU 1642

J Exp. Med (1998) 188, pp 619-626, Krause et al

Gene ther, (1995) Vol. 2. Suppl. 1:S19 (ISSN: 0969-7128. Cayeux et al

thank you,

Larry

R850.J6

STIC-ILL 273,499

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thank you,

Larry

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(FILE 'HOME' ENTERED AT 14:01:05 ON 06 DEC 1999)

FILE 'CAPLUS, CANCERLIT' ENTERED AT 14:01:23 ON 06 DEC 1999

L1	3874	S	CD28
L2	147	S	ANTI-GD2
L3	10413	S	THYMIDINE KINASE
L4	1	S	L1 AND L2
L5	3	S	L1 AND L3
L6	3	S	L1 AND L3
L7	598	S	SUICIDE GENE
L8	1	S	L1 AND L7
L9	0	S	L2 AND L7

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS
AN 1998:554622 CAPLUS
DN 129:259130
TI Antigen-dependent **CD28** signaling selectively enhances survival and proliferation in genetically modified activated human primary T lymphocytes
AU Krause, Anja; Guo, Hong-Fen; Latouche, Jean-Baptiste; Tan, Cuiwen; Cheung, Nai-Kong V.; Sadelain, Michel
CS Department of Human Genetics, Memorial Sloan-Kettering Cancer Center, NY, 10021, USA
SO J. Exp. Med. (1998), 188(4), 619-626
CODEN: JEMEAV; ISSN: 0022-1007
PB Rockefeller University Press
DT Journal
LA English
CC 15-2 (Immunochemistry)
AB Most tumor cells function poorly as antigen-presenting cells in part because they do not express costimulatory mols. To provide costimulation to T lymphocytes that recognize tumor cells, we constructed a **CD28** -like receptor specific for GD2, a ganglioside overexpressed on the surface of neuroblastoma, small-cell lung carcinoma, melanoma, and other human tumors. Recognition of GD2 was provided by a single-chain antibody derived from the GD2-specific monoclonal antibody 3G6. We demonstrate that the chimeric receptor 3G6-**CD28** provides **CD28** signaling upon specific recognition of the GD2 antigen on tumor cells. Human primary T lymphocytes retrovirally transduced with 3G6-**CD28** secrete interleukin 2, survive proapoptotic culture conditions, and selectively undergo clonal expansion in the presence of an antiidiotypic antibody specific for 3G6-**CD28**. Polyclonal CD8+ lymphocytes expressing 3G6-**CD28** are selectively expanded when cultured with cells expressing allogeneic major histocompatibility complex class I together with GD2. Primary T cells given such an antigen-dependent survival advantage should be very useful to augment immune responses against tumor cells.
ST T lymphocyte **CD28** tumor antigen presentation
IT Fusion proteins (chimeric proteins)
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**CD28-anti-GD2** scFv; tumor antigen-dependent **CD28** signaling selectively enhances survival and proliferation in genetically modified activated human primary T lymphocytes)
IT Immunoglobulin fragments
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**anti-GD2** scFv, fusion protein with **CD28**; tumor antigen-dependent **CD28** signaling selectively enhances survival and proliferation in genetically modified activated human primary T lymphocytes)
IT **CD28** (antigen)
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion protein with **anti-GD2** scFv; tumor antigen-dependent **CD28** signaling selectively enhances survival and proliferation in genetically modified activated human primary T lymphocytes)
IT Antigen presentation
Immunotherapy

Signal transduction (biological)
T cell (lymphocyte)
T cell proliferation
Tumors (animal)
(tumor antigen-dependent **CD28** signaling selectively enhances survival and proliferation in genetically modified activated human primary T lymphocytes)

IT Tumor-associated antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor antigen-dependent **CD28** signaling selectively enhances survival and proliferation in genetically modified activated human primary T lymphocytes)

IT Interleukin 2
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(tumor antigen-dependent **CD28** signaling selectively enhances survival and proliferation in genetically modified activated human primary T lymphocytes)

IT 65988-71-8, GD2
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(tumor antigen-dependent **CD28** signaling selectively enhances survival and proliferation in genetically modified activated human primary T lymphocytes)

L5 ANSWER 3 OF 3 CANCERLIT
AN 96606992 CANCERLIT
DN 96606992
TI Tumor cell vaccines using cells cotransfected cytokine (IL-4 or IL-7) and B7.1 genes (Meeting abstract).
AU Cayeux S; Beck C; Aicher A; Dorken B; Blankenstein T
CS Dept. of Medical Oncology and Tumorimmunology, Robert Rossle Klinik, Virchow Klinikum, Humboldt University, Berlin.
SO Gene Ther, (1995). Vol. 2, Suppl. 1:S19.
ISSN: 0969-7128.
DT (MEETING ABSTRACTS)
FS ICDB; L
LA English
EM 199605
AB Tumor cell vaccines using cytokine gene modified tumor cells are currently used in a number of clinical trials. Cytokines such as IL-2, IL-4, IL-7, GM-CSF and surface molecules such as B7 are both able to provide activation and proliferation signals for T cells. However, tumor cells transfected to express either molecules alone are not reliably rejected in syngeneic hosts or are not sufficiently immunogenic to serve as potent tumor vaccines. In two different syngeneic mouse tumor cell lines, one mammary adenocarcinoma (TSA) and one plasmacytoma (J558L), we have shown that vaccination with the combination of IL-4 and B7.1 or IL-7 and B7.1 eradicated tumorigenicity (not one single mouse developed a tumor when injected with tumor cells coexpressing IL-4/B7.1 or IL-7/B7.1). Moreover, immunization of mice with IL-4/B7.1 or IL-7/B7.1 cotransfected cells and subsequent contralateral challenge with parental tumor cells showed that coexpression of IL-4 or IL-7 and B7.1 on tumor cells induced strong systemic immunity superior to single gene transfectants and to the adjuvant C parvum/tumor cell mixture. Furthermore, irradiation of vaccine cells abrogated vaccine efficacy. Analysis of tumor infiltrating T lymphocytes revealed increased numbers of T cells in transfected tumor cells compared to parental tumor cells. But more importantly, there was a higher number of activated (**CD28**+ and CD25+) T cells infiltrating the cotransfected tumor cells. Thus, IIA or IL-7 and B7.1 in a cooperative fashion induced an antitumor immune response by complementary T-cell directed pathways. Taken together our results mean a step towards an improved tumor cell vaccine by the concerted action of cytokines such as IL-4 or IL-7 and B7.1 and the use of viable cells. Addition of the **thymidine kinase** gene as present in our B7.1 retroviral vector may provide the basis for a safe live tumor cell vaccine.
CN 0 (Antigens, CD80); 0 (Interleukin-4); 0 (Interleukin-7)